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BIOMEDICAL ENGINEERING AND INSTRUMENTATION BRANCH

DIVISION OF RESEARCH SERVICES

NATIONAL INSTITUTES OF HEALTH (U.S.)

ANNUAL REPORT FY 1983

Dr. Murray Eden, Chief

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1983

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DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10001-15 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pharmacokinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.L. Dedrick, Chief, ChES, BEIB, DRS

COOPERATING UNITS *(if any)*

CPB-NCI	NTP-NIEHS
North Dakota State University	SNB-NINCDS
Howard University	CP-CC

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2.5	2.5	

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and man. They provide a plausible set of equations that can be used to extrapolate data from animals to man and thereby improve chemotherapy, and risk assessment. Increased emphasis has been placed on regional drug administration, in particular intrathecal, intraperitoneal and intra-arterial. The former two modes have required the development of spatially distributed models of the tissue adjacent to the cerebrospinal fluid (CSF) or peritoneal fluid. These analyses have provided considerable insight into the penetration depths of drugs administered by these routes and the interpretation of CSF kinetics in terms of brain concentration profiles. The penetration of cis-dichlorodiammine-platinum (II) (DDP) into peritoneal and subperitoneal tissue is being examined experimentally with an electron probe and the results compared with a reaction-diffusion equation of the process. A lumped model of DDP pharmacokinetics is also being developed to include both metabolism to a mobile species and covalent binding to macromolecules. Pharmacokinetic theory has been developed for intra-arterial drug administration combined with hemoperfusion of vascular drainage, and the concepts have been validated experimentally in monkeys. A clinical trial is in progress.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10002-18 BEI

PERIOD COVERED
October 1, 1982 to September 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Implant Device Development

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
John W. Boretos, Physical Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
CR-CC; RO-NCI, Penn State Univ.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	.7	.3

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of the project is to elucidate the interaction of biomaterials used for specific implants with the physiological environment and to explore specially prepared biomaterials and design features with respect to their suitability and performance in a variety of contexts. For catheters designed to be used in the vascular system, thrombogenic events have been reduced by incorporating an anticoagulent at various levels within hydrogel layers which are attached to the surface. Slow release of the anticoagulant has significantly reduced the amount of clot generated on the surfaces as compared with untreated polyurethane catheters. Specific hydrogel formulations have been shown to reduce drag and eliminate sticking of catheters in the vascular system. A multi-lumen micro-catheter which is propelled and directed through small diameter blood vessels via jets of fluid emanating from its distal end has shown promise for negotiating heretofore difficult to reach areas. The catheter is controlled by an adjustable pressurized manifold operated by a joy stick. A transparent model of the vascular network simulating blood flow of a pulsatile nature was designed to evaluate the efficiency of the jet catheter system and its behavior in administering embolizing agents and chemotheropeutic drugs. Ex vivo studies of the polyurethane insulation of stimulating and pacing electrodes, along with long-term in vitro coupon studies have indicated reliable stability for segmented polyurethane for a number of surgical applications. Good correlation exists between in vivo and in vitro data for ultimate tensile strength and elongation over short-and long terms. Minor changes in physical properties when stored wet appear to be the result of a plasticizing effect which is reversible on drying. Segmented polyurethane stored in water with high bacteria counts over a 13 year period show up to 30% decrease in strength although the same material implanted in a sterile subcutaneous pocket for 3 years showed no appreciable changes. Our studies and that of others confirm that particles shed from the surfaces of in vivo and in vitro devices are not totally avoidable but can be minimized by careful control of the materials used for catheters, heart assist devices, injection sets, etc..

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
ZO1 RS 10015-08 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Toposcopic Catheter

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
D.R. Shook, Biomedical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
Diagnostic Radiology, CC

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
Division of Research Services, NIH, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.8	1	.8

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☒ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Toposcopy has been shown to be a viable means to catheterize small, tortuous vascular and gastrointestinal vessels. These regions have been inaccessable by existing techniques. Continuing developmental work will optimize catheter material properties, design parameters, and system configuration for diverse clinical applications.

The toposcopic element everts from the tip of a conventional catheter. This extremely flexible polyurethane element has been fabricated in 3, 4, and 5 French sizes mated with 5, 6, and 7 French catheters, respectively, and is capable of eversion lengths in excess of 30 cm. The present system design facilitates sterilization and maximizes safety, reliability, and reconfigurability for clinical investigations. The design of a completely automated system is underway.

Human use has continued from May 4, 1983 with the local delivery of a chemotherapy agent to brain tumors. Treatment is provided by positioning the conventional catheter in the internal carotid artery from a femoral entry, everting the toposcopic element through the carotid sinus and beyond the opthalmic artery to avert retinal toxicity, and perfusing the tumor through the middle and/or anterior cerebral arteries. Note that a conventional catheter cannot safely negotiate the tortuosity of the carotid sinus. Localized chemotherapy of other tumor locations, delivery of embolizing agents, and treatment of other vascular lesions are contemplated.

The toposcopic catheter is also under modification for gastrointestinal placement through the fiber optic endoscope. The toposcopic element has successfully negotiated the convoluted cystic duct, aspirating pure bile from a catheter entry at the exposed canine papilla of Vater. Envisioned uses for the catheter are sampling of pancreatic, gall bladder, and hepatic secretions for clinical research and infusions for dissolving gall stones in situ.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10018-08 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Particulate Hydrodynamics in Porous Membranes

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
P.M. Bungay, Chemical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
Department of Mathematics, University College, London, England

North Atlantic Treaty Organization, Brussels, Belgium

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.1	.1	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Mathematical models are being developed to describe passive membrane transport through pores or intercellular spaces junctions. The Taylor-Aris dispersion analysis is extended to treat combined Brownian motion and convection in a single pore. The solute particle dimension is assumed to be large compared to that of the solvent molecules and also appreciable in size compared to the lateral pore dimension. The latter condition implies strong hindered diffusion and related solute-membrane interaction effects. A key aspect of the analysis is a generalized Einstein relation for predicting axial and radial components of the diffusivity tensor from hydrodynamics solutions for resistance coefficients. Perturbation techniques are used to obtain asymptotic solutions to the hydrodynamic equations, and the method of moments is employed to analyze the solute continuity equation. Related hydrodynamic problems are also being considered, such as flow through constricted vessels.

The hydrodynamic results in combination with an analysis derived from irreversible thermodynamics, provide a predictive theory for simultaneous coupled convective and diffusive transport across porous membranes - either biological or synthetic.

A review of the theoretical approaches to transport in porous membranes is included in the curriculum for the North Atlantic Treaty Organization Advanced Study Institute on Synthetic Membranes; June 26-July 8, 1983, directed by the principal investigator.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10034-06 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Three-Dimensional Histological Reconstruction

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
S. B. Leighton, Mechanical Engineering, BEIB DRS

COOPERATING UNITS *(if any)*
LB NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.5	.45	.05

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A semi-automatic system for acquisition of three-dimensional structural information about histological material is being developed. The system should have significant speed and reliability advantages over present techniques using serial sections, although resolution may be limited. In brief, an embedded tissue block will be fixed relative to a scanning electron microscope imaging system, the surface of the block will be imaged and stored, and successive slices will be removed by a built-in microtome. Handling and registration of thin sections will thus be eliminated. Human and computer pattern recognition will transform the resulting set of images into a three-dimensional reconstruction. Oxygen plasma etching has been found to give sufficient topographic relief that the resolution of the images is now limited by the SEM and not by the preparation technique. The images of Hermissenda Crassicornis obtained by this technique correlate well with TEM images of the same tissue, indicating that the lack of artifact is adequate for the contemplated studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
ZO1 RS 10039-06 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biophysical Instrumentation and Methodology

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Marc S. Lewis, Research Chemist, BEIB/DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Microanalysis Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .2	PROFESSIONAL: .2	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project is designed to develop new instrumentation and methodology or improve existing instrumentation and methodology for characterization of biological macromolecules. Analytical ultracentrifugation, the techniques ancillary to it, and methods of data analysis using mathematical modeling appropriate for these techniques are the major areas of interest.

Improved precision and optimal efficiency in ultracentrifugal analysis requires improved methods of data acquisition. A microprocessor controlled data acquisition instrument for use with the microcomparator used for the measurement of photographic records from the ultracentrifuge has been developed earlier. The methods of data acquisition involved in the development of this instrument have been extended to the development of a system for the direct acquisition of data from the photomultiplier tube of the ultraviolet absorption scanner of the ultracentrifuge. The software requisite for making this system operational is currently in development. When complete, this system will permit direct acquisition of data while the ultracentrifuge is operating and then permit preliminary data processing followed by transmission of the data to the DEC-10 computer for detailed analysis. This will effect a marked increase in efficiency, significantly improved precision, enhanced facility in data analysis and will also more readily permit the effective modification of some experimental conditions such as rotor speed and temperature during the course of the experiment if the analysis indicates it to be desirable.

MLAB, operating on the DEC-10 computer, has been used for mathematical modeling studies for the analysis of various types of protein interactions. These studies have been applied to ultracentrifugal studies of binding and of protein self-association.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10040-06 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Physical Chemistry of Biological Macromolecules

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Marc S. Lewis, Research Chemist, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Microanalysis Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.8	PROFESSIONAL: 0.8	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to study the physical properties of a wide variety of biological macromolecules with the goal of correlating these properties to the structure and function of the macromolecules. The emphasis is on molecular size and shape and the thermodynamics of molecular interactions. Analytical ultracentrifugation and mathematical modeling are the principal research techniques used.

Extensive studies on the binding of plasminogen by fibrinogen have been completed. It has been shown that each fibrinogen molecule can bind four molecules of either the native glu-plasminogen or lys-plasminogen, a modified form produced by the plasmin or urokinase removal of a peptide with a molecular weight of 4000. The equilibrium constants for the binding of either of these two forms are virtually identical. It has been demonstrated that there is very marked cooperativity of binding for the third and fourth plasminogens bound, but the possibility exists that the binding of the second plasminogen may not involve such marked cooperativity. The net change in free energy for the binding of the four plasminogens is -33.5 kcal per mole of fibrinogen, indicating substantial hydrophobic interaction and probably significant structural alteration with binding. Calculations indicate that at physiological concentrations of these proteins, approximately one fibrinogen molecule in sixteen will have plasminogen bound to it and that molecule will most probably have four molecules of plasminogen bound. Studies are currently in progress on the association of plasminogen with plasmin inhibitor and on the association of plasminogen with the D and E fragments of fibrinogen.

Studies have been initiated on the associative properties of the alpha subunit of tryptpphane synthase. This protein, with a molecular weight of approximately 29000, can be split by limited trypsin proteolysis into two well characterized fragments with molecular weights of 20000 and 9000 respectively. It has been demonstrated that both of these fragments undergo reversible monomer-tetramer self-association. Studies are being undertaken to investigate the possible reassociation of the two fragments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10043-06 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Fiber Optic Probes

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
John I. Peterson, Chemist, BEIB/DRS

COOPERATING UNITS *(if any)*
H IR CB
H IR OD

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.6	0.6	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A suitable device is needed for the direct measurement of oxygen partial pressure (PO_2) in blood and tissue for both clinical and research applications. Methods currently available for measuring PO_2 lack convenience, reliability, speed, and relevance to many situations of interest. Efforts to develop electrical sensors have not been successful. It is desirable to have a very small PO_2 sensor which can be inserted into a blood vessel or tissue with little disturbance, and which will provide instantaneous and current PO_2 monitoring for either short or extended periods of time. A fiber optic sensor is ideal for this application, with the advantages, for physiological use, of very small size and flexibility, safety, and low cost.

A PO_2 probe was developed based on the principle of fluorescence quenching by oxygen. It consists of two 150 micrometer strands of plastic optical fiber ending in a section of porous polymer tubing about 3 mm long and 0.6 mm diameter. The tubing is packed with dye on an adsorptive support. The optical fibers are connected to a light source and measuring instrument which provide direct PO_2 reading. The general construction is similar to a pH probe previously developed here. Three major problems had to be solved: finding a suitable fluorescence indicator, devising an oxygen permeable container, and developing a support system for the dye which would activate it without humidity sensitivity. Appropriate instrumentation was developed for use and evaluation of the probe. The probe has been evaluated with in vitro and animal tests. There is considerable interest in application of the PO_2 probe, and instrumentation development for specific research projects is planned.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10050-05 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Positron Emission Tomography Scanner

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
W.S. Friauf, Section Chief, Electrical & Electronic Engineering Section, BEIB, DRS

COOPERATING UNITS *(if any)*
SN, NINCDS; MES, BEIB, DRS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical & Electronic Engineering Section, Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.7	PROFESSIONAL: 1.2	OTHER: .5

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☒ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A custom positron emission tomography (PET) scanner has been designed and built to provide characteristics tailored to the specific needs of NINCDS. During this year the full 7 slice capability has been implemented and the scanner has been in routine usage in conjunction with about a dozen clinical protocols. In addition, considerable effort has been applied to performance evaluation and to the suppression of several minor artifacts. This work will continue during the coming year, with particular emphasis on refinements of the spatial sampling program, interpolation, scatter correction, and elimination of ring artifact. It is also expected that animal studies at unusually high activity levels will be initiated, which will call for further study of several problems associated with very high count rates.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10053-05 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Membrane Based Sampling Systems for In Vivo and In Vitro Kinetic Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
P.M., Bungay, Chemical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
Laboratory of Medicinal Chemistry and Biology, DCT

Laboratory of Molecular Aging, NIA

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Chemical Engineerin Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .3	PROFESSIONAL: .2	OTHER: .1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Synthetic membranes are being utilized in kinetics studies to provide a means for continuous sampling of the liquid phases from systems in which a dispersed particulate phase is suspended in the liquid phase. In one application sampling equipment is being developed for in vitro study of calcium ion transport and calcium-ATPase activity in suspensions of sarcoplasmic reticulum vesicles prepared from homogenates of rabbit muscles. In a second application a study of the mammalian blood-brain-barrier permeability is being aided by the development of an apparatus incorporating a sampler in an arteriovenous ex vivo shunt. In the latter plasmapheresis application, pooling of the plasma filtrate yields a single sample from which the plasma concentration-times-time integral can be evaluated for a chemical administered to the animal. Such sampling systems can be useful for the study of the kinetics of other fluid phase systems for which a membrane can be found that is permeable to one chemical of interest but impermeable to another necessary reagent or sink. Thus, other applications might be found in the areas of enzyme kinetics, pharmacokinetics, and the membrane transport of vesicle and cell suspensions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10062-04 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
IEEE-488 General Purpose Interface Bus Program Development

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
T.R. Clem, Sr., Electronic Engineer, EEES, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.25	PROFESSIONAL: 0.2	OTHER: 0.05

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The increased availability and reduced cost of small desk-top computer has created increased interest in automating data acquisition and process or experiment control in areas where such things were not feasible before due to cost or complexity. With these changes also came a large increase in the use of the IEEE-488 GPIB by instrument makers. By combining the two, sophisticated instrumentation and data acquisition systems can be assembled quickly and inexpensively. The BEIB is continuing to develop the expertise to provide guidance and assistance to requirements where this approach provides the optimum solution. This capability is further assisted by the BEIB-SERP specifying the IEEE-488 interface on new equipment acquisitions whenever possible.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE
NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10064-04 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Indirect Blood Pressure Measurements in Laboratory Animals Using Oscillometry

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
E.C. Walker, Mechanical Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
SLAMS OD NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.75	PROFESSIONAL: 0.75	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Presently there are no reliable indirect methods of measuring blood pressure in dogs. Traditional techniques, used in humans, are unsatisfactory primarily because they require the placement of a transducer over the artery being monitored.

Because of the unreliability of traditional techniques we have been investigating a technique called oscillometry. Oscillometry is the method of measuring blood pressure by analyzing the pulse pattern of the cuff pressure oscillations.

In practice, a cuff is placed around a limb and inflated to a pressure above systolic and then slowly deflated. While the cuff is being deflated the amplitude of oscillation in cuff pressure, produced by the arterial pulse beneath the cuff, is monitored. Systolic and diastolic transitions in the oscillometric waveform are then used to indicate the indirect systolic and diastolic pressures respectively.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10065-04 BEI

PERIOD COVERED
October 31, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Transient Response of Micro-Calorimeter Using R-C Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*
LTD, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In earlier work, we developed an R-C model which enabled us to predict calorimeter performance within 5%. The model revealed several sources of error in the current calorimeter design. With this information, we re-designed the calorimeter to reduce these errors and to offer increased performance and flexibility. The re-design (a) eliminates the air gap, (b) requires only one sensor, (c) can accept all three currently used cell sizes 0.3, 0.5 and 1.0 ml, and (d) increases sensitivity with no significant change in rise-time. Preliminary experimental results show that the re-design achieves the performance predicted by the model.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10066-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Egyptian Training Project

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*
RIS, BEIB, DRS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.45	PROFESSIONAL: 0.45	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The development of a training program is medical equipment repair for Egyptian engineers. The goal is a completely self-sufficient training center in Egypt for recruitment and training of scientific equipment repair personnel. This project is specifcally concerned with the development of courses in basic instrumentation and electronics for scientific equipment.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10073-04 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Secondary Emission Mass Spectrometer

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Leonid Kelner, BEIB, DRS

COOPERATING UNITS *(if any)*
LCS NIMH and NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Microanalysis Group

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2.0	1.5	.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Secondary Emission Mass Spectrometer (SEMS) consisting of a particle bombardment ionization system (SIMS or FAB) coupled to a tandem quadrupole mass spectrometer has been developed and used to study various aspects of the secondary emission of organics sputtered by primary particles (Ar). On this system we have initiated a systematic study of the energetics of various organic ions in relation to the different experimental parameters which occur in the SIMS and FAB analysis of organics: (i) Primary beam - energy and nature of the primary particles, charge of primary beam, current density, static versus pulsed beam; (ii) Target conditions - type of material, target bias, orientation and conductivity; (iii) Nature of secondary ions - chemical structure, molecular weight, molecular ions, fragments, clusters, cationized molecular ions, etc.; (iv) Charge of secondary particles - positive, negative or neutrals. Some of these experiments have been performed this year and reported at the 31st Annual Conference on Mass Spectrometry and Allied Topics (Boston, May 1983). We have analyzed mixtures of various alkaloids and found that MS/MS technique combined with SIMS ionization could be a powerful method for analysis of mixtures of labile biological compounds. Our observation in the difference of the energy distribution of the sample and matrix ions (about 2 eV for m/z 272 of crinine and m/z 277 for glycerol) can be used as a novel method for supressing the interference signal from matrix by positioning an energy analyzer in the front of the quadrupole and preferentially focussing it (energetically) on the ion of interest. Continuation of these experiments will allow us to understand fragmentation and ionization processes of secondary ions under various conditions in SIMS instruments, analyze complex mixtures using particle induced ionization, obtain information on molecular weight and structure of various labile compounds of biological interest and design better conditions for efficient SIMS and FAB experiments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10076-04 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Elemental Analysis of Microdroplets

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
A.F. LeRoy, Chief, Analytical Methods Section, BEIB, DRS

COOPERATING UNITS *(if any)*
Department of Biology, Centre d'Etudes Nucleaires, Saclay, France

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Analytical Methods Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.5	PROFESSIONAL: 1.5	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The principal instruments used in this project are the Cameca MBX 2-50 KeV scanning electron beam microprobe and a Cameca MS-46 electron microprobe, each equipped with two wavelength dispersive spectrometers. Quantitative elemental analysis in volumes of the order of 10^{-10} liter are possible using these instruments. The signal for some elements changes with time as a function of beam current-density, sample mass thickness and some other characteristics of the samples. A systematic quantitative study of the variables that affect stability of the signal has been undertaken to establish the ranges of values of these variables that permit usable results to be obtained.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10082-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Protein Sequencer Modification

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Robert J. Lutz, Chemical Engineer, BEIB/DRS

COOPERATING UNITS *(if any)*
LCB, NCI
LI, NIAD

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .35	PROFESSIONAL: .35	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Proteins serve an incredible variety of biological functions which are determined indirectly by the amino acid sequence in the protein. The most effective single method for sequence determination is the degradation technique of Edman, which is performed by an automated instrument manufactured by Beckman. By a repetitive sequence of processes, amino acids are chemically cleaved one by one from the N-terminal end of a large protein or polypeptide. Recently, proteins of considerable interest are being isolated only in minute quantities, too small for accurate determination on available automated instruments. The goal of our project is to discover improvements to the present protein sequencing methodology that will allow for "microsequencing." The present emphasis so far has been to make improvements in the design of the Beckman automated sequencer. The three main features in the design that have been improved are (1) reagent and solvent delivery valve mechanism, (2) vacuum system, (3) automatic conversion of cleaved amino acid to a more stable phenylthiohydantoin derivative for analysis.

The modified Beckman sequencer is now being used to analyse proteins using 10 nmoles of sample with a repetitive yield of 95%.

The next approach is to investigate other types of automated instrumentation for handling sub-nanomole quantities of proteins and peptides, for example, miniaturized solid-phase systems or membrane-based devices for Edman reaction and product separation. A prototype for a membrane-based sequencer has been constructed and will undergo preliminary testing.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10095-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Multiple Probe pH Measurement System for Canine Myocardium

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
D. Markle, Biomedical Engineer, MES, BEIB, DRS

COOPERATING UNITS *(if any)*
Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering And Instrumentation Branch

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda MD 20205

TOTAL MANYEARS: 1.5 1.	PROFESSIONAL: .5	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

During the past several years, a miniature (0.5 mm diameter) fiber optic pH probe has been developed for physiological use. The first generation of probes and support equipment demonstrated the feasibility of optically measuring pH with a pH sensitive dye, and made many subleties associated with the probe construction and use apparent. The next generation of probes improved upon the original design to reduce their response time to a step change in pH to less than 60 seconds, to extend the range of the probe to between pH 6.5 and 8, and to provide for easy and atraumatic insertion of probes into the beating canine myocardium. Furthermore, the support system was changed to consist of a digital computer and associated hardware capable of collecting data from 5 probes simultaneously.

Within the past year, a seried of experiments using the improved fiber optic pH measurement system to measure pH in the contracting canine myocardium has provided cardiologists with in vivo, real-time measurements of intramyocardial pH. Such information is of use to experimenters interested in evaluating drugs which affect tissue perfusion, obstetricians interested in monitoring fetal scalp pH and biomedical researchers in general.

Recently, a new support system has been constructed which uses green/red LED's to replace the larger and more constly quartz halogen light source and motor-driven filter wheel of the second generation device. The new system utilizes a microprocessor to collect, analyze and display the data. Commercially available fiber optic connectors are now used and improved calibration procedures have been implemented.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10096-03 BEI

PERIOD COVERED
October 1,1982 to September 30,1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Light Scattering Method for Evaluation of Platelets

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.F. Bonner Physicist BEIB DRS

COOPERATING UNITS *(if any)*
Bureau of Biologics, FDA

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.4	PROFESSIONAL: 0.4	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Assessment of the functional status of platelets for transfusion is confounded by the inherent complexity of the cell, as well as the intricate requirements of sample preparation. A correlation between discoid shape and the functional integrity of the platelet has been established. We have developed a complex automatic machine based on previous experiments with a simple prototype which measures the fraction of the platelets that are discoid and the optical (volume) concentration of unaggregated platelets in standard blood bank platelet concentrate units within their bags. The microprocessor-based instrument automatically determines the volume concentration of unaggregated platelets and the fraction that are fully viable (discoid) during a 3-minute measurement sequence following simple insertion of the blood storage bag in the instrument. This process is noninvasive (sterile) and nondestructive. Thus it allows frequent measurements on the platelets prior to transfusion in order to optimize the quality and quantity of transfused platelets given patients. It also allows accurate investigations for optimizing storage and preparation methods.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10097-03 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Mechanics of the Left Ventricle and Myocardial Blood Flow

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.S. Chadwick, Biomedical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NHLBI - Cardiology Branch

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .3	PROFESSIONAL: .3	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A theory is presented for the mechanics of the left ventricle. A linear continuum description of the myocardium is developed, which incorporates anisotropic elastic effects due to the fiber direction field. The relation between fiber tension and fiber strain contains a time-dependent activation function that drives the ventricle around its cycle. The theory is applied to simplified geometry consisting of a thick-walled finite cylinder in which fibers spiral on helical paths and terminate on planar end surfaces. The helix pitch angle varies continuously through the wall. The ventricular cycle is analyzed by specifying the pressures at which the aortic and mitral valves open and close. Key quantities are tabulated which permit a simple determination of the properties of the model under changes of wall thickness, fiber angles, muscle parameters, preload, afterload, etc. It is shown how the active muscle parameters can be inferred from a measurement of the end systolic pressure-volume line.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10098-03 BEIB

PERIOD COVERED
October 1,1982 to September 30,1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Laser Instrumentation for Vitreous Surgery

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.F. Bonner Physicist BEIB DRS

COOPERATING UNITS *(if any)*
Clinical Branch, NEI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.8	PROFESSIONAL: 0.8	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study entailed the development of two different carbon dioxide laser systems (one was a prototype pulsed system with fiber optics delivery and the other was a modification of a commercial medical carbon dioxide laser). Additionally a prototype (mode-locked or Q-switched) pulsed Nd:YAG laser coupled to a slit lamp was used. These laser systems were tested in a series of animal experiments (in rabbits and monkeys) to test the efficacy and safety of cutting vitreal membranes. The carbon dioxide laser systems were designed to be an adjunct to standard mechanical vitreous surgery, whereas the Nd:YAG laser-slit lamp system was for more minor operations entailing the transection of selected membranes without incision to remove debris. For both types of laser systems systematic studies of animal vitrecomies were performed in order to characterize laser pulse characteristics necessary to transect vitreal membranes. Additional studies of retinal damage as a function of pulse characteristics and distance of cutting site from the retina clarified the potential for use of these laser systems close to the retina.

Preliminary data reveals that the carbon dioxide laser can cut experimentally created membranes in rabbits for virtually any condition of the clarity of the optical media. The Nd:YAG laser pulses can cut vitreal membranes when power densities exceeding 1 GW/cm^2 are achieved at the target. Moderate to severe turbidity of the optical media greatly decreases the ability to cut vitreal membranes with the Nd:YAG laser and create the potential for increased retinal damage. The Nd:YAG laser can not be used within 2 mm of the retina without significant risk of retinal damage due to the absorption of radiation by the outer retina. The CO_2 laser systems can be used within 2 mm of the retina safely only when short duration pulses are used at a slow repetition rate in order to prevent the establishment of convective currents of hot vitreous. The CO_2 laser is appropriate for cutting vascular membranes due to thermal coagulation of blood vessels accompanying the cutting action, whereas the use of the Nd:YAG laser in these cases without previous coagulation of vessels would result in vitreal hemorrhage.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10099-03

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cochlear Mechanics and Neural Modeling

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.S. Chadwick, Biomedical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NIADDK - Mathematical Research Branch

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda MD 20205

TOTAL MANYEARS: 0.1	PROFESSIONAL: 0.1	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study is concerned with a theoretical analysis of the propagation of mechanical waves in the cochlea, the traduction process in the cochlear hair cells, and the subsequent propagation of electrical impulses in the auditory nerve. In auditory physiology, both mechanical and neural processes play important roles. This study is intended to clarify their relative roles and interaction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10102-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Osmotic Behavior of Perfused Tissues and Organs

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.L.Levin, Biomedical Engineer, BEIB DRS

COOPERATING UNITS *(if any)*
MRC Medical Cryobiology Group, Cambridge University Department of Surgery, Cambridge, England

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, Maryland 20205

TOTAL MANYEARS: 0.40	PROFESSIONAL: 0.40	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to first study the osmotic behavior of perfused tissues and organs during the introduction and removal of cryoprotective agents (CPAs) and then to develop optimum CPA introduction and removal protocols. Currently, scientists at the MRC Medical Cryobiology Group at Cambridge University are experimentally monitoring the overall weight and venous outflow of rabbit kidneys perfused with solutions containing different types and concentrations of CPAs. At NIH, these data are being used in conjunction with a previously developed non-steady state mass transport model to deduce the permeability and elastic properties of the perfused kidneys. Continual comparison of the theoretical predictions of organ behavior during CPA introduction/removal with the experimental observations of the responses of perfused organs to changes in the composition of their perfusates hopefully will facilitate the development of optimum CPA introduction and removal protocol.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10103-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Triple Laser - Multi Parameter Flow Cytometry System for Study of Tumor Cell Kinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
W. Schuette, Chief, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*
DRS-NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3	2	1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A triple laser flow cytometry has been developed so that various immuno-fluorescent labeling techniques may be employed for the investigation of tumors cell kinetics. Three laser beams at different wave lengths are made to intersect a tumor cell flow stream passing through a quartz cuvette so that multiparameter signals may be obtained. These signals are processed by specialized electronics and then analyzed by means of a PDP 11 computer. Simplified optics have increased light detection efficiency by an order of magnitude.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10105-03 BEI

PERIOD COVERED

October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Adaptation of an EPICS II Flow Cytometer for T. Cruzi Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

T.E. Hall

COOPERATING UNITS *(if any)*

LPD-NIAID

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.8	.7	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An EPICS II FLow Cytometer is being used to perform cytometric analysis on a unicellular protozoan known as trypanosoma cruzi, the causative agent of Chagas disease. The EPICS II is composed of a fluid flow system for hydrodynamic focusing, a laser for excitation, signal processing electronics for data acquisition and a computer for data analysis. Developmental work is being carried out upon this system in order to improve the quality of the data acquired and the way in which it is analyzed. This includes modification of the various sensing systems to increase signal to noise ratio and the interfacing of a graphic display system in order to expand the data processing capability.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10106-03 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Molecular Uptake in Tumors Using Chronic, Implanted Fiber Optic Probes

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Ronald L. Levin, Biomedical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
LPP-NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.0	PROFESSIONAL: 0.2	OTHER: 0.8

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Using an in vivo micro-fluorimetry system previously developed, we have employed carboxy fluorescein and fluorescently-tagged dextran tracers in an attempt to characterize the mass transport characteristics of solid tumors. Some of the tissue signals could be analyzed with a simple linear model by deconvolution with the associated blood signals to provide intercompartmental transport parameters; others showed a more complex behavior. Comparison of our transport data with histological studies of random tissue samples support the hypothesis that tumor mass transport is spatially heterogeneous.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE
NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10109-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Adjunct Heat Treatment of Cancer

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R. L. Levin, Biomedical Engineer, BEIB DRS

COOPERATING UNITS *(if any)*
Radiation Oncology Branch, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 2.0	PROFESSIONAL: 2.0	OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to facilitate the development of adjunct hyperthermia modalities for cancer treatment by theoretically and experimentally studying the spatial and temporal variation in the temperature field of tissues subjected to microwave and radio-frequency electro-magnetic radiation. Currently, we are mathematically modeling the electromagnetic energy deposition characteristics and resulting thermal profiles of human extremities subjected to RF irradiation from various types of helical coil applicators. We are also conducting experimental measurements of the thermal profiles of various types of phantoms subjected to RF irradiation from various types of helical coil applicators. We have found (1) that helical coil applicators operating under self-resonant conditions can produce deep, relatively uniform and stable heating in fat-muscle phantoms and (2) that they should be able to locally raise the temperature of an extremity to the therapeutic temperature range of 42-45°C. In preparation for developing a clinically useful system, our coil design, phantoms, and bio-heat transfer model are currently being optimized.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10110-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Dual 3-Dimensional Position Monitor For Speech Analysis: MOD. II

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
E. C. Walker, Mechanical Engineer, ACES BEIB

COOPERATING UNITS *(if any)*
LCD-NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 2.5	PROFESSIONAL: 2.0	OTHER: .5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Several speech monitoring instruments have been designed to study the etiology of normal and abnormal articular movements in humans. The first system, which is in current use, provided a unique method of monitoring 3-D lip and jaw movements. The second system, MOD II, is an improved version of the first. The device consists of two, mirror image, transducers mounted on a common head frame. Each transducer, which can be individually adjusted, is capable of measuring the movement of a point in three orthogonal planes. The transducers have been structurally and operationally redesigned to provide increased linearity, resolution, and reduced weight. Additionally, the head frame has been totally redesigned to provide improved wearing comfort and reduced weight. The improved system will facilitate studying a broader patient population such as children and the elderly.

Design and fabrication of MOD II has been completed. Results of bench tests indicate that the system performes well, within its specified range. Future efforts will be directed toward patient testing.

PHS 6040 (Rev. 1/83) GPO 895-100

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10112-03 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Analysis of Microcirculatory Blood Flow by Laser Doppler Scattering

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.F. Bonner, Physicist, BEIB, DRS

COOPERATING UNITS *(if any)*
Lab. of Technical Development, NHLBI; Lab of Clinical Investigation, NIAID; Lab of Chemical Biology, NHLBI; Allergy and Rheumatology Depts., Walter Reed Army Medical Center; MED Pacific, Inc., Seattle, Washington.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.1	1.1	

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is the development of a clinical, non-invasive monitor of tissue blood flow by analysis of the spectrum of Doppler scattered laser light. The NIH Laser Doppler Blood Flow Monitor has been demonstrated to be highly portable and clinically convenient with sterilizable, rugged flexible 4m fiber optic probes and portable and photodiode detection system. The linearity of the flow analysis processor has been demonstrated in a variety of tissues and clearly resolves physiologic flow changes including instantaneous pulsatile flow in the microcirculation. Muscle blood flow in over 50 patients with neuromuscular disease has been studied and data suggest that post occlusive reactive hyperemia responses may be primary or secondary indicators of disease state. Measurements of local muscle blood flow dynamics in patients with neuromuscular diseases indicate abnormalities distinct to different disease types. Nasal Blood flow has been shown to be a quantitative measure of the physiologic response of the nose to allergic and drug challenges. Scleroderma patients fingertip blood flow appears to fall in three easily-discernable classes asociated with the severity of the disease and a simple measurement protocol may elucidate efficacy of drug therapy. Preliminary studies show a characteristic local oscillatory flow pattern in a capillary microcirculation of the skin in sickle cell patients which appears to correlate with severity of disease and its reponse to drug therapy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10114-02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Phasic Aortic Pressure Control System for Awake Dogs

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
S.R. Goldstein, Chief, MES, BEIB, DRS

COOPERATING UNITS *(if any)*
Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.8	.5	.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A system is being developed which will control phasic aortic pressure in awake closed chest experimental dogs. Aortic pressure can either be manipulated on a beat to beat basis in an arbitrary manner, or a waveform can be captured and then reproduced over an extended period of time. A typical use of the system will involve evaluating the effects of a drug intervention where the pressure waveform before the intervention is reproduced after the intervention, thus allowing changes in inherent muscle contractility to be observed apart from changes in systemic pressure. A modification of the system will be developed to control end diastolic filling pressure.

Aortic pressure is manipulated by a feedback controlled gas filled intra-aortic balloon catheter which resides in the descending aorta and is used in conjunction (when necessary) with a speed controlled roller blood pump. The pump bypasses the systemic circulation via catheters to provide the DC and low frequency control whereas the rapidly responding balloon provides the high frequency control. Aortic pressure at the outlet of the heart is measured with a catheter tip pressure transducer and fed back via an electronic controller to move a linear motor which positions a bellophragm which in turn inflates or deflates the balloon. The hardware has been bench tested and will shortly be evaluated in experimental dogs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10116-02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Modeling of Arterial Pulse Waves

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.S. Chadwick, Biomedical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NHLBI, Endocrine-Hypertension Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .6	PROFESSIONAL: .6	OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A new theory was developed to compute the propagation of the pressure wave in a branching system. The theory includes cross sectional area and stiffness variation, viscous and viscoelastic effects, and side branch flow. The theory was then used in an analytical model of the brachial artery system which can reproduce the phasic pressure waveforms as measured in normal and hypertensive subjects. Particular emphasis was directed toward an understanding of the genesis of the peripheral dicrotic wave, and its modulation by vasoactive drugs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10117-02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Optimum Cryoprotectant Introduction/Removal for Blood Components

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.L. Levin, Biomedical Engineer, BEIB/DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.10	0.10	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to first study the osmotic behavior of platelets and other blood components during the introduction and removal of cryoprotective agents (CPAs) from both an experimental and analytical point of view and then to develop optimum CPA introduction/removal protocols which can be readily employed in blood banks. Currently, the osmotic response and functional integrity of platelets and other blood components are being experimentally observed by scientists at the Cryobiology Laboratory of the American Red Cross Blood Research Laboratory. At NIH, the theoretical predictions of cell behavior during CPA introduction and removal based upon a previously developed non-steady state mass transfer model are being compared to the experimental observations of the responses of cells to changes in the composition of their suspending media. This correlation of our experimental and analytical findings permits the relevant transport parameters (e.g. cell water permeability, cell solute permeability and cell solute reflection coefficient) to be deduced. On the basis of these results, a modified dialysis system which will be capable of altering the CPA content of platelets and other blood components in a controlled manner is also being designed. With such a system and a previously developed theoretical method for optimally introducing and removing CPAs, it is hoped that osmotic stresses and strains imposed upon cells during conventional introduction/removal protocols can be minimized.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10122-02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Mini-computer Controlled Fermentation System

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
T.R. Clem, Sr., Electronic Engineer, EEES, BEIB, DRS

COOPERATING UNITS *(if any)*
LCDB - NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.0	PROFESSIONAL: 0.5	OTHER: 0.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A process control system using a small desktop computer as the central control element is continuing to be developed for the NIH Fermentation Pilot Plant. The various monitoring transducers and controlled elements (pumps, valves, etc.) are connected to the computer via the IEEE-488 General Purpose Interface Bus (GPIB). For maximum versatility most components used are commercially available items (instruments, meters, etc.). The GPIB-based design allows changes in the parameters measured or controlled, or scaling to different size vessels to be accomplished relatively quickly and easily. Utilizing the computational capabilities of the computer/controller allows initial selection of the operating parameters and dynamic alteration of these parameters as the process continues, thus allowing optimization of yields or detailed study of the process parameters.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10125-02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Automatic Assessment of Cytochrome P450

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R. F. Bonner, Physicist, BEIB DRS

COOPERATING UNITS *(if any)*
Laboratory of Chemical Pharmacology, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .10	PROFESSIONAL: .10	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continuous flow analyzer has been designed and tested for use wth a programmable dual channel spectrophotometer. The system allows continuous monitoring of a chromatography column output containing cytochrome P450 by comparing the difference spectra at 420, 450, and 490 nm of the reduced form and that reacted with carbon monoxide. The current prototype resolved 10 nanomolar Cytochrome P450 in a resolved measurement volume of 0.8 ml.

PHS 6040 (Rev. 1/83) GPO 895-100

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10126-02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Trace Analysis and Elemental Microanalysis in Biological Materials

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
A.F. LeRoy, Chief, Analytical Methods Section, BEIB, DRS

COOPERATING UNITS *(if any)*
CPB-NIMH; LCM-NHLBI; LCP-NIAMDD; LMP-NCI; ICIG-Villejuif, France; Biophysics Department, Medical Faculty of Creteil, University of Paris.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Analytical Methods

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
4.0	4.0	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Flameless atomic absorption spectrophotometry (FAAS) and neutron activation analysis (NAA) have been used for quantitation of vanadium, platinum, calcium, iron, cobalt and some other elements in biological tissues and fluids. The analyses are important in clinical biochemical, pharmacokinetic, and binding studies. Very sensitive analytical techniques are necessary because, in some instances, the elements are present in trace concentrations (i.e. typically in the part-per-million (10^{-6} g/g) or part-per-billion (PPB) (10^{-9} g/g) level and less frequently at the part-per-trillion (PPT) (10^{-12} g/g) level, and, in many cases, the sample size is small as well (i.e. less than 1 ml). Elemental Electron Probe Microanalysis has been performed using a Cameca MBX instrument equipped with a transmission microscope (Creteil, France) to localize several elements, platinum, iron and sulfur on the microscopic scale in different tissues. Separation techniques including ion-exchange chromatography, solvent extraction, and electrophoresis have been used to purify samples, fractionate and concentrate chemical species before analysis, and eliminate substances interfering with trace level assays.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10132-02 BE

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Image Processing and Cell Classification

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J.R. Ellis, Expert, BEIB/DRS

COOPERATING UNITS *(if any)*
SNB/NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Office of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.85	0.75	0.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In vitro cell culture is an effective method for the study of the effects o chemotherapeutic agents on neurological tumors. Quantitation of all but the most rudimentary of these effects is generally beyond the ability of human observers Thus, an automated system for acquisition of image data, extraction of parameters o interest, and statistical processing of results is necessary for any quantitativ effectiveness.

Historically, this field has been qualitative. Thus, moving toward quantitativ evaluations has involved a very broad spectrum of discussions about methods, limitation of methods, desired results, and significance of results. Specifically, it i necessary to prepare cultures and micrographs differently for human visual inspectio and for reliable machine processing. In addition, it has been necessary to clarify th strong and weak points of human and automated image processing.

This has been especially important in this project because the system originall purchased was ill-suited to the tasks envisioned and support from the manufacture was totally inadequate. Thanks largely to the efforts of C. C. Gibson of BEIB, th system has been substantially rebuilt and made much more reliable and capable.

In vitro cytotoxicity assays of the effects of AZQ, BCNU, and other drugs on Glioma tumor cell lines using cell counts over titer plates have become a reliable productio operation. Morphology studies, using size, aspect ratio, and a shape factor have begu on micrographs of granules and mitochondria.

These studies should be continued over the next year, with FORTRAN supplanting BASIC as the computer language of choice.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10135 02 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
The Effects of Fluid Shear on Cultured Endothelial Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.J. Lutz

COOPERATING UNITS *(if any)*
American Red Cross
FDA

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	.4	.6

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Many pathophysiological processes in the cardiovascular system such as thrombosis, vessel wall injury, and atherosclerosis occur in the presence of fluid shear forces. These shear forces have a direct mechanical effect on the vessel wall and can also indirectly affect wall properties by mediating the interactions of blood elements with the lumenal surface. The normal integrity of a vessel wall is maintained by a delicate monolayer of endothelial cells on this lumenal surface. The aim of this project is to investigate the interactions of fluid shear forces with the vessel wall surface by utilizing endothelial cells grown in monolayer culture in a specially designed flow chamber. Morphological, cytoskeletal, and metabolic changes in the endothelial cells are being investigated as a function of fluid shear stresses on the cell surface. The flow chamber consists of a parallel plate geometry which accomodates Thermanox circular cover slips upon which human umbilical cord endothelial cells are cultured. The flow patterns and shear stress values within the chamber have been characterized using electrochemical shear measurements,flow visualization techniques, and laser doppler anemometry during steady flow. We have tested the chamber at shear stresses up to 20 dynes/cm^2. The flow remains laminar in the test region over the cover slips. Laser Doppler velocity profiles have characteristic parabolic shape. Both the velocity profiles and the measured shear agree to within 10% of theoretical values for parallel plate flow. With no flow, the cells form a random pattern of cobblestone cells with no orientation. Little or no orientation is observed at shear stresses from 4 to 7 dynes/cm^2 up to 72 hours. At 8 to 12 dynes/cm^2, cell orientation is observed by 48 to 72 hours. At shear stresses from 12 to 16 dynes/cm^2, the cells have orientatd within 24 hours. A radio-immunoassay is being developed to measure the production of von Willibrand factor and Factor VIII during shear experiments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10136-02 BE

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Imaging in Positron-Emission Tomography

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J.R. Ellis, Expert, BEIB/DRS

COOPERATING UNITS *(if any)*
NM/CC

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Office of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.35	PROFESSIONAL: 0.25	OTHER: 0.1

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Positron-Emission Tomography (PET) and emission computed axial tomography (ECAT) offer unprecedented opportunities to visualize and measure in-vivo organ metabolism. Our current interest centers on the brain, perhaps the least accessible region of the body to non-invasive diagnostic probes.

One desiragle goal of image processing in this field of interest is determination of volumetric metabolica activity from collections of scan plane data. Our work on data spreading and attenuation due to finite object size (partial voluming) has made specification of object recovery as a function of system resolution possible. Thus, axial sampling can be chosen to maintain visibility of, or activity recovery from, objects of a selected minimum size through a set of scan planes.

With such choices, it is possible to relate scan plane data to a three dimensional model of the brain robustly. Use of such a model can allow meaningful comparisons of data taken from subjects with different orientations and locations relative to the PET or ECAT frame of reference.

Another, more ambitious, goal is to make a dynamic model of brain activity. Then, one can use time-series PET or ECAT data to estimate biological quantities in functional compartments. Further analysis allows estimates of the parameters of the kinetic rate equations relating them.

Work is underway on these topics.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10137-02 BE

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Processing of Electron Microscope Images

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J. R. Ellis, Expert, BEIB/DRS

COOPERATING UNITS *(if any)*
CSL/DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Office of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.75	1.75	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An overall goal of the DRS-BEIB/DCRT-CSL Electron Beam Imaging and Microspectroscopy (EBIM) Project is to obtain chemical elemental maps of biological samples with resolution in the sub-micron range which are subjectively satisfying and objectively meaningful. Our image processing work associated with this project has developed with essentially four foci: Quality enhancement, pixel value and uncertainty estimation, controlled parameter image generation, and provision of a sufficiently friendly user interface for a user to employ tools developed to meet the goals of the first three points. Our quality enhancement for a set of images with dissimilar characteristics includes making them compatible for comparison and for overlays and other forms of composition by expansion, contraction and smoothing. It also involves construction of collages or montages from several images, background subtraction, region edge enhancement, and matching of desired signal ranges to the eye's response.

Significant new analytical and simulation results have been obtained on the statistical variations to be expected for EEL elemental edges and X-Ray elemental peak-to-background ratios. Work on improved pixel value estimation is in progress.

Synthetic images with controlled parameters are being used very effectively in resolving questions of object visibility and artifact generation. A statistically-based effort directed toward automatic region definition and image segmentation is underway.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10143-02 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Interaction of Body Temperature and Sleep Rhythms

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
T. L. Talbot, ACES BEIB DRS

COOPERATING UNITS *(if any)*
Psychobiology Lab-NIMH

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.8	0.7	.1

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Clinical evidence suggests a correlation between core body temperature and the frequency of sleep episodes. An artificial thermoregulatory system is completed which will enable core body temperature manipulation. This devices permits the evaluation of the efficacy of thermal regulation in the treatment of sleep disorders. Clinical trials are now performed on a regular basis. Simultaneous sleep recordings are obtained during both a non-manipulated and manipulated 24 hour period.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10145-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Opthalmodynamometry: Correlation with CSF Pressure

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
S.B. Leighton, Mechanical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
SN, NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .1	PROFESSIONAL: .1	OTHER: 0

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☒ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Opthalmodynamometry is a standard non-invasive technique for measuring correlates of intraocular pressure. A theoretical mechanical model will be developed to relate CSF pressure and modified opthalmodynamic pressure. The model will be tested by making opthalmodynometric measurement on patients who are already having CSF pressure monitored invasively. As necessary, the model will be adjusted, and it will be determined to what extent the technique is a useful clinical measure of CSF pressure. A modified opthalmodynamometer will be constructed to make these measurements.

PHS 6040 (Rev. 1/83)

GPO 895-100

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10146-01 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Prosthetic Urethral Sphincter

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
S.B. Leighton, Mechanical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
DCT,NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .1	PROFESSIONAL: .1	OTHER: 0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A number of techniques are used for treating urinary incontinence, including a number of artificial prosthetic sphincters. The present work concerns an entirely intraurethral artificial sphincter that can be implanted without surgery. Concepts are being explored which would allow the device to be used in situations in which surgery is contraindictated, and would also presumeably lower the cost. The valve would be appropriately matched to urethral dimensions, pressures, and flowrates. The valve would be potentially useful in cases of nonopening normal valves as well as in cases of non-closing valves.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10147-01 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Viscoelastic Properties of the Erythrocyte Membrane

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Aydin Tozeren, Visiting Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
Bioengineering Institute, Columbia University, New York; A-LCP

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.30	PROFESSIONAL: 0.30	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The erythrocyte membrane is modelled as a two dimensional viscoelastic continuum that evolves under the application of stress. The present analysis on the erythrocyte membrane is motivated by the recent development of knowledge on its molecular structure and by its complex behavior exhibited in dynamic micropipette testing and in tank treading during shear flow. The proposed constitutive equations have the form similar to that of a two dimensional Kelvin model with a constant area condition. However, the membrane viscosity is made to depend on the rate of strain and the elastic strain tensor is measured from the evolving preferred configuration. The evolution of the preferred configuration is given by a rate equation. The material constants appearing in the proposed constitutive equations may be useful indicators of the biochemical state of the membrane in health and disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10148-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Analysis of the coupling between left ventricle and vascular system

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Richard S. Chadwick

COOPERATING UNITS *(if any)*
Cardiology Branch, Surgery Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.35	PROFESSIONAL: 0.35	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The aim of this study is to develop equations governing left ventricular pressure and volume during a cardiac cycle. It is assumed that the stress in the myocardium is composed of an isotropic tissue pressure term and fiber tension. Fiber tension T depend on the stretching and rate of stretching of cardiac fibers as well as an internal variable c that describes the degree of electrochemical activation of the muscle fiber. Using mechanical equations of equilibrium and the constitutive equations mentioned above, a time dependent pressure-volume relation is obtained for the left ventricle. Hydraulic characteristics of the large arteries are modelled by a three parameter windkessel model. It is assumed that the aortic pressure is equal to the ventricular pressure P when the aortic valve is open. Mechanical events of the cardiac cycle are considered by using the developed model. Functional relationships are explored among the parameters identifying the contractility of the left ventricle, the resistance and compliance of the vascular system, and the experimentally observed quantities such as pressure, flow rate, etc.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10149-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Constitutive Equations of Skeltal Muscle Based on Cross-Bridge Mechanism

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Aydin Tozeren, Visiting Scientist, BEIB

COOPERATING UNITS *(if any)*
NIADDK, LPB

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.35	0.35	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Statistical mechanics of cross-bridge action is considered in order to develop constitutive equations that express fiber tension as a function of degree of activation and time history of speed of contraction. The kinetic equation of A.F. Huxley (Prog. Biophys. Mol. biol. 7:255, 1957) is generalized to apply to the partially activated state. The rate parameters of attachment and detachment, and cross-bridge compliance are assumed to be step functions of extension, x, with a finite number of discontinuities. This assumption enables integration of the kinetic equation and its moments with respect to x analytically resulting in equations where x has been eliminated. When the constants in the rate parameters and the force function are chosen such that Hill's force-velocity relation and features of the transient kinetic and tension data can be fitted, the resulting cross-bridge mechanism is quite similar to the one proposed by Podolsky and co-workers (Proc. Natl. Acad. Sci. USA, 64:504, 1969). Because the derived constitutive equations simplify mathematical analysis, they enable the evaluation of the influence of various cross-bridge parameters on the mechanical behavior of muscle fibers. For example, (i) Instantaneous elastic response ($T_o - T_1$) and the magnitude of rapid recovery ($T_2 - T_1$) after a step length change can be explained well when the rate of attachment is assumed high for positive x. In that case T_2 corresponds to the force generated by cross-bridges in the region of negative x. (ii) Kinetic transients occur as a result of the jumps that exist in the distribution of attached cross-bridges during the isometric state. Because of the hyperbolic nature of the kinetic equation, these jumps propagate in the -x direction causing rapid changes in the speed of contraction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10150-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cardio-vascular Instrumentation System

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
G.M. Maxwell, Staff Fellow, BEIB, DRS

COOPERATING UNITS *(if any)*
Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch, DRS

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.15	.15	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An instrumentation system is being developed to provide geometric measurements of the canine vertrical. Different configurations of ultrsonic crystals are being explored, which, when combined with a theoretical model of the ventricle will yield on line volume information. Both global and local measuring techniques will be examined. Signal processing and storage systems are being developed so that other variables, e.g. left ventricle pressure, etc. together with appropriate time derivations can be simultaneously studied. Other parameters such as contractility, p•/p etc will be studied.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10151-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Nuclear Magnetic Resonance Imaging

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Dr. David I. Hoult, Physical Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
Department of Radiology, Clinical Center

LAB/BRANCH
NMR Imaging Laboratory, Biomedical Engineering and Instrumentation Branch

SECTION
Office of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, Maryland 20205

TOTAL MANYEARS: 3.8	PROFESSIONAL: 3.5	OTHER: 0.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In the past year considerable progress has been made in refining the nuclear magnetic resonance (NMR) image equipment to the point where it has produced images of resolution 0.7mm, in 3mm thick phantoms, in 77 seconds. Both the sensitivity and the speed of data processing (under 3 seconds for an entire image) are unmatched in any other instrument. Images were produced with a technique unique to this laboratory (rotating frame zeugmatography) which shows enormous potential, both in terms of versatile performance and economy. The method requires neither gradient coils nor costly switched power supplies, and the machine can be operated with a stabilizer and field frequency lock. It thus has relative immunity to the movement of ferrous objects nearby. Basic research has been performed on improvement of sensitivity for the technique of NMR imaging in general, and a probe system has been developed (for use in high field, superconducting installations) which uses 50% less radio frequency power and which delivers 40% better sensitivity. During the year, the research group has been active in educating and assisting the Radiology Department of the Clinical Center in preparation for the installation of a commercial imaging machine. Future research will concentrate on improving our slice selection techniques, on obtaining three dimensional and flow images and on applying our experience to the commercial instrument in a clinical setting.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10152-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Measuring and Imaging Magnesium in Lymphocytes by Electron Beam X-ray Microanalysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
G. Hook, Staff Fellow, Clinical Pathology, Clinical Center

COOPERATING UNITS *(if any)*
Clinical Pathology, Clinical Center

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Offfice of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.0	PROFESSIONAL: 1.0	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Magnesium is a cellular element essential for bioenergy transformation and macromolecular structures. It is required for bone formation, nerve conduction, muscle contraction and sodium and potassium homeostasis and has been implicated in heart disease. However, direct experimental data on magnesium variation between individual cells and magnesium distribution within a cell have not been available. This work applied the new method of computer controlled, electron beam x-ray microanalysis to quantitate magnesium variation between individual cells and study subcellular magnesium distribution.

Preliminary data indicate that the magnesium content in individual lymphocites can be determined and that subcellular magnesium distribution can be imaged. The relative amount of magnesium in individual cells has been shown to vary. Experiments are underway to study synchronized cell populations to determine magnesium variation as a function of mitosis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10153-01 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Position Sensor for Computer Modeling

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
H.E. Cascio, Electronic Engineering, BEIB, DRS

COOPERATING UNITS *(if any)*
CCB, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health

TOTAL MANYEARS: .25	PROFESSIONAL: .15	OTHER: .10

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For the study of macromolecular structure and of molecular interactions, the use of a computer generated display of the molecule is a powerful interpretive tool. In particular, the ability to be able to manipulate in space, i.e. to rotate and translate the molecule(s) to any desired orientation enhances the usefulness of the device. A further degree of sophistication is to provide a feedback mechanism giving an indication of the repulsive or attractive forces (Van der Waals interactions) present as two molecules are fitted together or as a single molecule is twisted to a new conformation. A joy stick apparatus is being designed to provide these features. Two molecules or part of the same molecule can then be rotated and translated in any direction. With each new position, the computer program re-evaluates (on a one millisecond timescale) the appropriate forces to provide the investigator with a feel of the total forces involved.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10154-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Photo-Irradiation of Cancer Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
P.D. Smith, Visiting Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
NCI-VB, NCI-DCT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.5	PROFESSIONAL: 0.5	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Investigations of the interaction of light and hematoporphyrin (HP) for the killing of cancer cells has been carried out. The enhancement by selected agents to augment the photo-induced HP killing effect has been evaluated.

Previous work indicated that for leukemic L1210 cells (10^6 cells/ml) in vitro the most efficient wavelength for killing (assessed by trypan blue exclusion) was 503 nm, which corresponds to one of the HP absorption peaks. In addition, the presence of succinyl acetone in the medium (in addition to the HP) was found to enhance the effectiveness of this photo-induced killing. Additional agents which are known to alter membrane properties, chloroquine and dibucaine, have also been found to produce an enhanced effect: e.g. addition of 10 M chloroquine to the medium produced an order of magnitude increase in cell death after 3 days relative to HP alone. The mode of action of this enhancement has not been determined. Other attempts, using the singlet oxygen trap, -carotene, and the anti-oxidants, vitamins C and E, to implicate singlet oxygen as the cytotoxic agent have proven inconclusive.

In vivo studies on mice of inter-peritoneal irradiation using fiber optic probes connected to an argon ion (514nm) laser head are being established. This laser line, as noted above, is close to a major absorption peak which has been found particularly effective for cell killing. The experience gained with the enhancing agents of the photoinduced HP effect will be applied where appropriate to this study.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10155-01 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Vidicon Detection for Fluorescence Microscopy

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
H.E. Cascio, Electronic Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
KE, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .35	PROFESSIONAL: .25	OTHER: .1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For one dimensional spectral analysis of the fluorescent properties of kidney microtubules, a vidicon detector has been mounted at the image plane of a microscope. The Princeton Applied Research model 1216/1254 detector is ideally suited for this application in that the scanning parameters of the vidicon are readily adjustable to provide the optimum configuration for the viewed image. However, for initial sample set up, and for two dimensional data collection, the lack of a standard video mode is a limitation. A modification has been made to this detector to produce an optional standard composite video signal. The existing preamplifier in the model 1254 detector is a charge sensitive preamplifier which integrates the video signal across each horizontal scan line. This integration causes a loss of resolution in the horizontal direction, when used in the standard video mode. A fast video preamplifier was designed and placed inside the preamplifier housing with the original preamplifier. A command from the computer terminal selects the scanning mode and connects the proper preamplifier into the system.

PHS 6040 (Rev. 1/83)

GPO 895-100

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10156-01 BE

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Differential Scanning Calorimeter

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*
A LMB, NIADDKD

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.10	PROFESSIONAL: 0.10	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
 ☐ (a1) Minors
 ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The transfer of sensor design and modelling techniques to the field of differential scanning calorimeters from earlier work in differential heat conduction calorimeters offers the promise of an improved design with faster scanning time and higher sensitivity than current designs. The first phase consists of modeling the new designs to optimize the performance while the second phase consists of implementing the design into hardware and evaluating it experimentally.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10157-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Temperature Controlled Chamber for X-ray Diffraction Specimens

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*
DCRT, CR-PSL

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.10	PROFESSIONAL: 0.10	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The development of a system to isolate a protein sample in a vacuum (10^{-2} atm) chamber and control the temperature of the sample to within ±0.5°C over the range 10°C to 50° while the sample is exposed to an x-ray beam to obtain diffraction patterns.

PHS 6040 (Rev. 1/83) GPO 895-100

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS10158-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Isolate Heart Perfusion

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
M.A. MacCollum, Mechanical Engineer, ACES, BEIB, DRS

COOPERATING UNITS *(if any)*
Surgery Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.9	PROFESSIONAL: .8	OTHER: 1.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An apparatus for perfusion of isolated rat hearts has been developed which circulates a buffered blood analog. This device is used to investigate biochemical and physiological parameters of the heart, including blood pressure, pulse pressure, cardiac output, tissue pH and others. The system allows investigators to induce temporary cardioplegia, during which pharmacologic agents may be introduced into the modes of operation: working heart, ischemia (both warm and cold) and Langendorf aortic perfusion. Comparing the pre- and post-plegic parameters allows the investigators to assess the ability of certain drugs and procedures to sustain cellular life through ischemic periods.

The results gained from the isolated heart experiments will be tested in large animals in vivo, using the same parameters along with animal survival after surgery.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10159-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pathophysiology of Cachexia in Sarcoma Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R. Corsey, Electronic Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
SURG NCI, ANES NCI, DCT NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Indirect calorimetry is used to study the metabolic demands active tumors have on cancer patients. A rigid lucite head canopy with a controlled air flow rate, an on line mass spectrometer and a computerized data processing system will be utilized. Stable isotopes will be used to measure whole body protein turnover and muscle and tumor fractional synthesis rates. Primary objectives are to determine if resting energy expenditure glucose oxidation, whole body protein turnover and K40 levels are different from controls in preoperative sarcoma patients. Of further interest is whether these parameters correlated with tumor size or protein fractional synthesis. The value of these parameters will again be measured after resection of the tumor.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10160-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Heat Treatment Apparatus for Treatment of Leishmaniasis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R. Corsey, Electronic Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
LPD NIAID

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.3	PROFESSIONAL: 0.3	OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Previous work has established hyperthermia as a desirable method of treatment of Leishmaniasis, a skin disease caused by protozoan parasites. Feasability studies have used hot water based equipment in which heated water was circulated through pads placed next to the skin lesions. This water-based equipment was bulky and inconvenient for transport and use in tropical areas where the disease is manifest. This project will produce a totally electric system which can be used in the field (tropics) and at NIH. It will utilize feedback control and overheat cut-out and will be packaged for convenient transport and multiple power sources.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10161-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Clinical Engineering Program for Hospital Patient Care Areas

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R. Corsey, Electronic Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
OD CC

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.5	PROFESSIONAL: 0.5	OTHER:

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This program has evolved from the Electrical Safety Program for patient care areas. It is designed to preventative maintenance for patient care equipment, electrical safety testing for equipment both clinical and research in nature, and electrical safety for patient care areas. Auxiliary services provided are incident investigation for equipment failure and misadventures, and education of medical and support personnel regarding equipment hazards and guidance for utilization of electronic technology in patient care. In addition this program assures hospital compliance with patient care electrical standards of the Joint Commission on Accreditation of Hospitals and the Health Care Facilities section of the National Electric Code.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10162-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Wound Healing: Biology and Rheology

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Thomas Talbot, ACES, BEIB

COOPERATING UNITS *(if any)*
DRS, NCI, University of Pennsylvania, Philadelphia VA Hospital, PA

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 1.3	PROFESSIONAL: 1.0	OTHER: 0.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A large population of animal models for **wound healing** will be studied. Past studies in this area have dealt with the effects of **biologic** or **mechanical** intervention during the wound healing process. This project is designed to simultaneously study both the **biological** and **rheologic** aspects of the healing mechanism. Correlates between the **impressed strain** and the **wound breaking strength (WBS)** will be sought after. The inter-relationship between WBS and pharmocologic agents introduced internally or subcutaneously are to be studied. Both **rat models and swine models** will be used to further substantiate any significant findings.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10163-01 BEI

PERIOD COVERED
October 1,1982 to September 30,1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Magnetoencephalography for Localization of Foci of Neurologic Activity

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

R.F. Bonner	Physicist	BEIB DRS

COOPERATING UNITS *(if any)*
Epilepsy Branch, NINCDS; Naval Research Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.2	PROFESSIONAL: 0.2	OTHER:

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study entails the development of a SQUID magnetic field gradiometer and methodology for its use to localize the three dimensional coordinates of the foci of neurologic activity in the brain particularly those associated with epileptic discharges. Through collaboration with the Naval Research Laboratory, preliminary studies of the localization of alpha wave foci in normals and the observation of the magnetic field correlates of focal EEG spike discharges in epileptic patients were begun. Methodologies for analyzing the MEG signals and the correlation of MEG and EEG activity as well as mapping protocols are being developed. The specification of a multichannel array of magnetic gradiometers suitable for routine clinical measurements is to be based on the preliminary measurements with a one channel device.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10164-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Distribution of Phosphorus and Calcium in Newly Formed Bone

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Richard D. Leapman, BEIB, DRS

COOPERATING UNITS *(if any)*
Mineralized Tissue Research Branch, NIDR

LAB/BRANCH
Biomedical Engineering And Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda MD 20205

TOTAL MANYEARS: 0.3	PROFESSIONAL: 0.3	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In mineralized tissue research it is often useful to carry out experiments on in vitro tissue cultures. For example, various compounds can be added to investigate their effect on bone formation. It is extremely important to characterize the in vitro tissue and to compare its composition with that of normal in vivo tissues. Electron energy loss spectroscopy is being used to find the relative distributions of phosphorus and calcium in cultured mouse condyle. Preliminary results indicate that the composition of certain newly formed mineralization samples is different from that of hydroxyapatite.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

ZO1 RS 10165-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
EELS Study of Invasion of Red Blood Cells by Malaria Parasites

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
R.D. Leapman, BEIB, DRS

COOPERATING UNITS *(if any)*
Laboratory of Parasitic Diseases, NIAID

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch, DRS

SECTION
Electron Beam Imaging and Microspectroscopy Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .2	PROFESSIONAL: .2	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The membranes of erythrocytes invaded with certain malaria parasites (plasmodium falciparum) contain knoblike structures which cause the cells to be trapped in capillaries, resulting in high morbidity and mortality rates. Little is known about the composition of the "knobs" which are about 100 mm in size. Analytical electron microscopy is being applied to thin sectons of monkey erythrocytes invaded with malaria to search for iron in possible concentrations of heme, and nitrogen in regions containing possible concentrations of histidine. It is planned to label histidine with fluorine to localize this compound in the cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10166-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Detection of Foreign Particles in Lung Tissue

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Richard D. Leapman, BEIB, DRS

COOPERATING UNITS *(if any)*
Pathology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda MD 20205

TOTAL MANYEARS: 0.2	PROFESSIONAL: 0.2	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Electron energy loss spectroscopy and X-ray emission spectroscopy have been used to analyze foreign particles in electron microscopy samples taken from lung biopsies and lavages of Clinical Center cases with known exposure to various reagents. In several cases chronic granulomatous lung disease was present. Thin sections of tissue in the granuloma regions showed the presence of particles in macrophages. In one case of exposure to volcanic ash, alumnosilicates were found; titanium was found in another case where exposure had been suspected. The particles which ranged in size from 20 to 200 nm were also imaged with X-rays so that an elemental map could be superimposed on a scanning transmission micrograph. This type of microanalysis is the only method available for identifying such small particles embedded in tissue, and demonstrates a useful clinical application of the analytical electron microscope.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10167-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Low Z Imaging of Chromaffin Cells by EELS

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Richard D. Leapman, BEIB, DRS

COOPERATING UNITS *(if any)*
Laboratory of Cell Biology and Genetics, NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Hitachi 200 KeV analytical electron microscope can now produce EELS elemental maps of the low Z elements, carbon, nitrogen and oxygen, which constitute most of the mass of a cell. Since the relative numbers of these atoms vary from one cellular compartment to another, significant information should be contained in C, N and O images. In order to learn how low Z imaging can be applied to cell physiology, carbon and nitrogen maps have been obtained from the well characterized bovine adrenal chromaffin cells. In particular the secretory granules, which are important in the production and exocytosis of epinephrine, have been imaged for nitrogen and carbon. The granules are shown to rich in nitrogen, probably due largely to nucleotides, but some nitrogen defficient regions are evident which can be correlated with membrane-bound compartments in the STEM micrographs. The granule membranes are apparent in the carbon image. It is intended to extend the study to cells which have been treated with fluorine labeled catecholamines. Detection of fluorine would greatly extend the usefulness of the method.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10168-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Software for Quantitation of EELS

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carol R. Swyt, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.3	PROFESSIONAL: 0.3	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Software for the automatic quantitation of electron energy loss spectra recorded with the Kevex multichannel analyzer has been developed. This makes use of a data base of characteristic edge energies and parameters so that many spectra can be analyzed very rapidly. The software includes a computation of the ionization cross sections and allows an absolute measurement of the concentration of elements in a thin section.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10169-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Software for Electron Energy Loss Imaging

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carol R. Swyt, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.2	PROFESSIONAL: 0.2	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects
  ☐ (a1) Minors
  ☐ (a2) Interviews

☐ (b) Human tissues

☒ (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In the recording of electron energy loss elemental maps, the background spectrum at each pixel of the image must be subtracted from the measured signal above a characteristic core edge. Previously, other laboratories involved in this work have used only one channel for the background estimation. However since the shape of the background is known to change as a function of sample mass thickness, the resulting images have been liable to contain artifacts. New software has therfore been written to test the effects of mass thickness on the energy loss images, recorded with the Hitachi 200 keV analytical electron microscope. It is possible to predict when artifacts will occur and to correct for them, and in doing so improve the statistics in the elemental maps.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10170-01 BEI

PERIOD COVERED
October 31, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biological Applications of a Computed Controlled Analytical Electron Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Richard Leapman, BEIB, DRS

COOPERATING UNITS *(if any)*
Computer Systems Laboratory, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 3.0	PROFESSIONAL: 3.0	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

After promising preliminary results were obtained from energy loss and x-ray elemental maps with the Hitachi 200 keV analytical TEM-STEM, it was necessary to improve the performance and stability of the system to make applications to biological problems possible. Such improvements have led to increased sensitivity and improved ease of operation. A new high voltage power supply has been incorporated into the energy loss spectrometer deflection plates so that a 1000eV range of energy loss can be covered in a single image. New data acquisition software, run by the LSI 11-23 satellite computer, has been written to compensate for spectrometer drift by "locking on" to the carbon edge in the energy loss spectrum. This enables images to be acquired over periods of one hour or more. Extensive software (K.E. Gorlen, DCRT) has been developed for the automation of data acquisition incorporating video display menus run from the DEC PDP 11/60 computer. Various parameters required for data acquisition are entered into "forms" so that the operator always has an updated list of values. Additional software has been written for use with the DeAnza image processor system. This allows the user to display and operate on the images using a "digitizing-tablet". Operations such as obtaining histograms, enhancing constrast or scrolling may be achieved very rapidly in this way. It is now possible to acquire not only the number of core edge counts at each pixel but also the parameters for the background fit. This allows more sophisticated data analysis to be carried out with concomitant reduction in noise and higher sensitivity. Improvements have also been made in the energy dispersive x-ray imaging. A digital filter is applied to the spectrum and the computer sums the filtered counts in each peak of interest at each pixel to determine the intensity. Artifacts due to mass thickness can be removed in this way. Apart from these software developments, improvements in the microscope are also in progress. A cryotransfer specimen holder (purchased from Gatan) should allow samples to be maintained at close to liquid nitrogen temperature with high mechanical stability. Experiments on frozen hydrated thin sections are proposed to study the distribution of low atomic number elements in cells.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10171-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Electro-optic Element for Projection of 3D Movies

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
P.D. Smith, Visiting Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
DCRT, CCB

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .4
PROFESSIONAL: .3
OTHER: .1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Computer generated structures of macromolecules displayed on a video monitor are an extremely useful method of studying the shape and function of molecules. The user is able to visualize pockets within the molecule, its binding sites, and regions of strain leading to instability, etc. This usefulness is further enhanced when the user can rotate the molecule at will to any desired orientation so that a particular region of interest can be studied from several viewpoints.

A major limitation of such a display system is that it is limited to those facilites with sufficient computing and displaying power capable of presenting the images. An attractive approach to allow these structures to be more readily available is to make a 3-D movie rotating the molecule from several aspects, concentrating on specific areas of interest.

An apparatus has been designed and constructed to permit viewing, using polarized glasses, these 3D movies. The apparatus, which is inserted into the beam in front of the projection lens, can be used with any projector. It consists of an electro-optic element which, on application of a predetermined voltage, rotates the plane of polarization of the transmitted projected light by 90°. The movie, which consists of alternate views of the macromolecule from the left and right eye perspective, is frame synchronized with the voltage switching of the electro-optic element. Thus each frame is projected in alternating perpendicular polarized light; the viewer, wearing eyeglasses with orthogonal polarizations for each eye, perceives a 3-D effect. Since the frame rate of the movie has been effectively halved, the movie flickers to a certain extent, but not sufficiently to reduce the 3-D effect or of the "movie" image.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10172-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Portable Programmable Drug Delivery System

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C. Wooten, Electronic Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NICHHD, LDN

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.4	.3	.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A battery operated microprocessor system, using low power CMOS technology, provides control of a portable infusion pump. This programmable system is compact enabling a patient to wear it, and it provides sufficient power for drug infusion periods up to one week. A major feature of the controller is the ability to program a fairly complex infusion sequence in contrast to the standard repetitive sequence delivery systems which are available. Programming variables are the time of day for infusion, the infusion duration, the rate of infusion during the infusion period. These variabled are entered via a keypad in response to prompts given on a display which in normal operation shows, the time of day. The ability to be able to establish a defined infusion pattern allows the drug delivery to be correlated with the biological clock. The system is not restricted to any particular drug infusion schedule and can be applied to many drug delivery applications.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10173-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Computer Control of Electron Beam X-ray Microanalysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C. Fiori, Physical Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
CSL, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Offfice of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 3.0	PROFESSIONAL: 3.0	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The new system of computer controlled electron beam x-ray microanalysis is being applied in several biological areas. This system, developed by BEIB and DCRT, produces digital images of small samples, 1 m^2 to 1mm^2, which contain elemental and structural information. Elements in the sample heavier than boron can be imaged and the micro-elemental distribution correlated with surface and transmision electron microscopic structural images. Elemental information is obtained from the characteristic x-rays emitted by the electron beam and sample interaction and collected by wavelength dispersive or energy dispersive x-ray detectors. The computer controlled acquisition, storage and display system maps the number of signal counts for each picture element and thus, the intensity of each picture element is directly proportional to the collected signal. Digital imaging allows image processing to correct for analytical artifacts and enhance fine details and image quantitation to extract quantitative data from regions of interest in the image.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10174-01 BEI

PERIOD COVERED
October 1982 to September 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Display and Response Tester for Amnesic Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
C. Wooten, Electronic Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NIAAA, LCS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical & Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.5	.4	.1

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A display and response tester has been designed and constructed for use in testing amnesic patients. In this study, the subjects ability to retain new information, which in this case takes the form of picture images, is being assessed for amnesic patients relative to normal control subjects. Further correlation of the mental activity stimulated by the visual image is being undertaken with brain scans performed on the PET scanner.

For the testing, a sequence of single images is presented as a study set to the patient which is followed by another sequence of image pairs, one of the images in that pair was present in the study set. The patient is to select which one this was and his response is recorded. Previously, testing was performed using slide projectors to perform this task; however, unreliable operation and auditory stimuli associated with the change mechanism provided a distraction. The present system uses a microprocessor controller to drive a video tape recorder and a video display unit providing an easy to use, trouble free presentation. In addition, the controller also records the responses made by the patient and compares their final response with the correct response for accuracy. A print-out of the number of responses with timing for each image, as well as the accuracy of the response, is given at the end of the session. Further, as an aid to the examiner, a run time display is used to monitor whether or not the patient is responding to any given image. For each testing sequence a unique video tape is used, which after insertion into the unit releases the operator to perform other duties; previously the operator was required to constantly monitor the slide projectors and to change the slide trays at the appropriate point. The tester has the necessary hardware to make each video tape, and uses the audio track to label each picture for identification of responses in the testing mode.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10175-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Semi-Automated Electrophoresis Gell Reader

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carter C. Gibson, Electronics Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NCI, Division of Cancer Cause and Prevention

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.2	.1	.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Dr. James Lautenberger and his group had to have a way to read electrophoresis gels of various DNA and RNA sequences without looking up from the gel plate as many mistakes were being made bacause they were losing their place in the sequence. Our laboratory desinged and built a device that interfaces to a DEC-MNC computer that has a 12 button keypad with a cursor on it to keep your place as you scan the gel plate. As each key is pressed, corresponding to the element of the sequence, it is entered into the computer and the key pressed is spoken back to the operator. Thus, allowing backing up and correcting an improper entry without looking away from the gel. The unit is inexpensive and easy to implement. The unit is under evaluation now and several more may be built.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10176-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Laboratory Studies of the Biology of Malignant T Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carter C. Gibson, BEIB, DRS

COOPERATING UNITS *(if any)*
NCI, Navy

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical Engineering Section

INSTITUTE AND LOCATION
National Instutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .25	PROFESSIONAL: .2	OTHER: .05

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

To check the results of maglignant T cell work being done by Dr. P.A. [illegible]unn Jr. at NCI, Navy a Coulter Cell Sorter with an 8 bit microporcessor is being used. While this machine is fine for collecting data it is painfully slow at analysing the data. To correct this problem DCRT has developed the LASAL interface and a large collection of programs to analyze the data to run on a Dec PDP11/34 using RT-11. The major problem with this system is that DCRT is no longer going to support LASAL in its present form and that the LSASL requires a trigger input which the Coulter system does not provide. To use the LASAL, the external trigger required using standard N.I.M. Bin modules. We have also provided a parallel interface between the Coulter system and the PDP11/34 so that the Coulter system can aquire the data and the PDP 11/34 system can analyze the data. Work is still being done on the software for storing the data on the PDP 11/34 is a format compatible with DCRT's programs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10177-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Computerized Cell Counting and Morphology

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carter C. Gibson, Electronics Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NINCDS, SNB

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical & Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .5	PROFESSIONAL: .4	OTHER: .1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

DRS, Barry Smith and Paul Kornblith of NINCDS, Surgical Neurology Branch have begun using a computerized light microscope to do in-vitro cytotoxicity studies and computerized electron scanning microscope to do chemotherapeutic cell monphology studies. Our laboratory has extensivily expanded the computer (a Data General Nova) so that the system will be more user friendly and much more complicated analysis may be done. Several design flaws have been discovered and corrected. A separate printer channel has been added and two high speed CRT's have been added. Momory has been expanded to the maximum so that two tasks may be run concurrently.

At present only one level of thresholding may be done and additional hardware has been ordered to allow 256 levels of thresholding and display. The electron microscope interface will be replaced with a more general purpose one that will be connected to the SEM and their 200 kv STEM. An interface is also planned for the energy dispensive x-ray analzer allowing elemental images to be collected. Most of the software will have to be rewritten to handle the new hardware. The cell counting is now being done on a production basis and the cell monphology studies are being done on a routine basis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10178-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Exocytosis Modelling: Kinetics of Memebrane Aggregation and Fusion

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carter C. Gibson, Electronics Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NTS, NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical & Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .35	PROFESSIONAL: .3	OTHER: .05

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For Stephan J. Morris, NS, NINCDS, we have constructed a computer controlled multisignal rapid-mixing stopped-flow apparatus. This unit consists of a lamp source, wavelength monochromator, an Aminco-Morrow stopped-flow assembly, and 3 photomultipliers with their associated electronics. One photo-multiplier tube measures optical density at a particular wavelength of light and the other two photo-multipliers measure fluorescence at different wavelengths and polarizations.

The electronics is designed to condition four signals, providing variable gain, offset, and switchable low pass filtering. Channel one is for optical density two and three and for the fluoroescence signals, and the fourth is the lamp output signal which is used to normalize the other three channels the outputs of the four amplifiers are then input to a Dec-PDP 11/34 computer which is triggered by the stopped-flow apparatus and collects four channels of analog data at a variable rate and plots all four channels in real time. The data are then saved on disc and then is transferred to a VAX 11/780 for the analysis of the kinetics of membrane fusion of phosphalipid vesicles. Work was also done by BEIB on data analysis on the DEC 10. The programs developed are for the PDP 11/34, written in Fortran for ease of maintenance, consist of about 2000 lines of code for the data acquistion program, and about 1000 lines of code for a program to replot the data and print the file variable information. Future work will be to add a dual wavelength monometer and syncronization to use it.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10179-01 BEI

PERIOD COVERED
October 1, 1982 to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Controller for Rapid Freezing of Tissue

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carter C. Gibson, Electronic Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
NIADDK, Laboratory of Cell Biology and Genetics

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical & Electronic Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: .25	PROFESSIONAL: .1	OTHER: .15

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

BEIB built a new controller for a rapid tissue freezing device. The device cools a 100 n liter sample of tissue from room temperature to liquid helium temperature in less than one millisecond. The old controller had unstable timing and the magnet and solenoid driver circuits were not fast enough or powerful enough. The new controller has been evaluated and two more are being constructed for various labs at NIH.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10180-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Imaging Calcium and Aluminum Deposits in Brain By Electron Beam X-ray Microanalysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
G. Hook, Staff Fellow, Clinical Pathology, Clinical Center

COOPERATING UNITS *(if any)*
NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Offfice of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.5	PROFESSIONAL: 0.5	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Aluminum and calcium deposits have been demonstrated in brain tissue of patients with Alzheimer's disease, progressive dialysis dementia, amyotrophic lateral sclerosis and parkinsonian-dementia by x-ray microprobe analysis. However, in these previous studies, aluminum and calcium were not imaged and the distributions of these elements were not well characterized. This work applied the computer controlled, electron beam x-ray microanalysis system to image aluminum and calcium in the hippocampus of patients with these diseases. Aluminum images obtained from such cases clearly show high concentrations of aluminum in neurofibrillary tangle-bearing neurons (NFT), a pathological cell type associated with these conditions. Calcium images show calcium has the same distribution as aluminum and is concentrated in the NFT neurons. The graphical information produced by this work clearly demonstrates that the aluminum and calcium are sequestered in NFT neurons, the distributions of the elements overlap and provide further evidence correlating high concentrations of aluminum and calcium with specific pathological structures in these diseases.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 10181-01 BEI

PERIOD COVERED
October 1, 1982 through September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Imaging and Quantifying Platinum Distribution by Electric Beam X-ray Microanalysis

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
G. Hook, Staff Fellow, Clinical Pathology, Clinical Center

COOPERATING UNITS *(if any)*
Clinical Pathology, Clinical Center

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Offfice of the Chief

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS: 0.5	PROFESSIONAL: 0.5	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Cis-platin (Cis-Pt) is a chemotherapeutic drug useful in the treatment of ovarian cancers. Chemical engineering studies are currently being conducted on the pharmokinetics of cis-Pt administered by peritoneal lavage. Of special interest is the distribution of cis-Pt penetration from the peritoneal surface into the abdominal wall. This work applied computer controlled, electron beam x-ray microanalysis to image and quantitate the Pt distribution in the abdominal wall of rats given cis-Pt by peritoneal lavage. Preliminary images of abdominal wall sections show platinum can be imaged. The distribution of platinum is of interest in modeling cis-Pt uptake in the abdominal wall.

VETERINARY RESOURCES BRANCH
DIVISION OF RESEARCH SERVICES
NATIONAL INSTITUTES OF HEALTH

FY 1983 VRB ANNUAL REPORT

Dr. Robert A. Whitney, Jr., Chief

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DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00001-13 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Animal Model Development

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Carl T. Hansen, Geneticist, SAS, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: 0.6	PROFESSIONAL: 0.33	OTHER: .27

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The nature of these projects are long term, therefore, the progress made each year is incremental. The project to establish a gene which when homozygous results in obesity in rats in two different inbred strains has yielded a model which may have potential for the study of adult onset diabetes mellitus. The evidence suggests that the resulting diabetes is the consequence of the underlying resistance to insulin rather than obesity per se since the disease was apparent only in the insulin resistant strain but not in the insulin senstitive strain. The preliminary results of a second study concerned with the development of immunodeficient mice by establishing mutations which affect the functioning of the immune system suggest that these mice may have promise for cancer research and parasitology since their immune systems appear to be quite similar to animals which have been severely immunocompromised by the use of chemicals. Additional studies are currently underway for confirmation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00002-12 VR

PERIOD COVERED

October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Development of Diets for Laboratory Animals

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

J.J Knapka, Nutritionist, SAS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: 1.1	PROFESSIONAL: 0.1	OTHER: 1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continuing program in laboratory animal nutrition involves various stocks and strains of rats, mice and guinea pigs as well as various species of nonhuman primates. A series of factorial designed feeding trials are used to ascertain the nutrient requirements of the animals involved and to develop diets with more nearly optimal nutrient concentrations for their growth, reproduction, maintenance or general health status. This program has resulted in the development of open formula natural ingredient diets for various species of small laboratory animals which are currently being used throughout NIH and the entire biomedical research community. Diets most recently developed are for nonhuman primates and toxicology studies with mice and rats. Currently work is continuing to develop diets for marmosets and for maximum reproduction in the inbred guinea pig.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00029-06 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Clinical Pathology Studies of Animal Health Conditions

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
E. J. Baas, Chief, CU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .5	PROFESSIONAL: .3	OTHER: .2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Studies are being conducted to define and characterize spontaneous diseases occurring in the NIH canine colonies. Preliminary clinical investigation has identified some disease problems. Hematological and chemical tests are being performed. The purpose of these investigations is to improve the quality of animals and animal products provided for research and characterize models of disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE
NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00030-06 VR

PERIOD COVERED
October 1, 1982, to September 20, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Evaluation of Mycobacterium paratuberculosis Bacteria in the Goat

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Martin L. Morin, Chief, PRU, VMSS, VRB, DRS

COOPERATING UNITS *(if any)*
National Animal Disease Laboratory, Agriculture Research Service, Ames, Iowa

LAB/BRANCH
Veterinary Resources Branch

SECTION
Veterinary Medicine & Surgery Section and Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .02	PROFESSIONAL: .01	OTHER: .01

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study is designed to determine if a bacterin against Johne's disease will affect the incidence and age of onset of the disease in goats. One-half of the kid goats produced by NIH Animal Center conventional does in 1978 and 1979 were vaccinated at one month of age and are being observed for life.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00034-06 VR

PERIOD COVERED

October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Reproductive Physiology of Selected Exotic Nonhuman Primates

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

D. M. Renquist, Chief, PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .6	PROFESSIONAL: .2	OTHER: .4

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study is to establish breeding systems for producing healthy Aotus, Saimiri, Saguinus, and Cercopithecus in a consistent manner for research investigators at NIH and other interested scientists. Basic reproductive parameters being studied include duration of gestation, male and female reproductive cycles, accessory sexual organ development, male-female breeding ratios, reproductive hormone serum levels, puberty changes, infant development, and minimum reproductive age.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00036-06 VR

PERIOD COVERED

October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Genetic Profile of the NIH Inbred Mouse Strains

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

H.A. Hoffman, Chief, Genetics Unit, Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*

Small Animal Section, VRB, DRS

LAB/BRANCH

Veterinary Resources Branch

SECTION

Comparative Pathology Section

INSTITUTE AND LOCATION

Division of Research Services, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project has been discontinued because the principal investigator is no longer an NIH employee.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00042-05 VR

PERIOD COVERED

October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Development of a Standard Strain of Mice for Pertussis Vaccine Bioassays

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

K.P. Smith, Geneticist, Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*

Pertussis Branch, National Center for Drugs and Biologics, FDA

LAB/BRANCH

Veterinary Resources Branch

SECTION

Comparative Pathology Section

INSTITUTE AND LOCATION

Division of Research Services, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	0.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this project is to develop a standard strain of mice used for pertussis vaccine bioassays. Two lines of mice have been selectively bred for their susceptibility and resistance to sensitization by the histamine sensitizing factor (HSF) of Bordetella pertussis and have been designated HSFS/N and HSFR/N. After 20 generations of selection, the ability to be sensitized by HSF in the HSFS/N line has increased to 70 percent, and in the HSFR has decreased to 0.5 percent. The two lines have been further characterized for 12 biochemical isozymes.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE
NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00043-05 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Micromethods for Cytotoxicity Testing in the Laboratory Mouse

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J.S. Crowell, Jr., Staff Fellow, Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Comparative Pathology Section

INSTITUTE AND LOCATION
Division of Research Services, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .5	PROFESSIONAL: .5	OTHER:

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to develop techniques for rapidly typing the cell surface antigens expressed on lymphocytes from various strains of mice. A variety of methods using both vital dye exclusion and radioisotope release are being explored.

Initial objectives have been attained and a manuscript is in preparation. Future requirements and modifications of this technique will be made as part of normal program developments.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00046-05 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Evaluation of Donor Safety in Leukopheresis of Canines

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
E. J. Baas, Chief, CU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
Blood Products Branch, Division of Blood and Blood Products
Bureau of Biologics, FDA

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .6	PROFESSIONAL: .2	OTHER: .4

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Leukopheresis on canine blood donors is being conducted to determine if repeated removal of lymphocytes affects the immune response. Information obtained on the maximum frequency or total number of leukopheresis donations is to be extrapolated for human donors.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00047-05 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Screening Laboratory Animal Diets for Chemical Contaminants

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J.J. Knapka, Nutritionist, SAS, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.15	.05	.10

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continuing program is being conducted for the routine analyses of feed samples for chlorinated hydrocarbons, polychlorinated biphenyls, organophosphates, lead, arsenic, cadmium, mercury, nitrate and aflatoxins. A sample collected from each batch of animal feed manufactured under NIH contracts is submitted to an independent laboratory for assay. The objective of this program is to document the concentrations of these contaminants in the natural ingredient diets purchased for use at NIH and to accumulate data that could be used as a basis to establish maximum permissible concentrations in laboratory diets and to ascertain which of these are a real problem.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00051-04 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Reproduction in Mutant Sheep Used for the Study of Hyperbilirubinemia

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
L. D. Stuart, Chief, UU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
Digestive Diseases and Nutrition Program, National Institutes of Arthritis, Metabolism and Digestive Diseases.

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.2	.1	.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A specific genetic strain of Corriedale sheep is used as an animal model for the study of liver pathophysiology, specifically, hyperbilirubinemia (Dubin-Johnson Syndrome). This project is concerned with increasing the numbers of animals available for research by the controlled breeding of individuals which genetically transmit this character. This project is utilizing what is considered to be the only existing Corriedale sheep homozygotic for this trait. Efforts are being made to obtain both homozygous and heterozygous offspring from these highly inbred individuals. Semen collected artificially from rams is diluted in various cryoprotective extenders and then freeze preserved. This will ensure the long-term availability of male gametes for artificial insemination. Overall, this project allows perpetuation of this specific gene pool and ensures availability of research animals for future investigations of Dubin-Johnson Syndrome and related metabolic disorders.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00056-04 VR

PERIOD COVERED

October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Mandibular Analysis as a Means of Discriminating Inbred Strains of Mice and Rats

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

H.A. Hoffman, Guest Worker, Comparative Pathology Section, VRB, DRS

COOPERATING UNITS *(if any)*

Small Animal Section, Veterinary Resources Branch, DRS
Laboratory of Statistical and Mathematical Methodology, DCRT

LAB/BRANCH

Veterinary Resources Branch

SECTION

Comparative Pathology Section

INSTITUTE AND LOCATION

Division of Research Services, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	0.8	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is designed to determine the ability of the mandibular analysis to discriminate between inbred strains of mice and rats maintained by the VRB. Discriminant Analysis, Canonical Correlation Analysis, and Computer Image Analysis are being used to analyze data from 20 inbred strains of mice. Preliminary studies conducted during FY 1983 have yielded encouraging results. It appears likely that this methodology may be capable of distinguishing even closely related strains such as C57BL/6 and C57BL/10. Work during the forthcoming year will focus on the ability of mandibular analysis to discriminate between inbred and hybrid animals.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00062-03 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Investigation of fetal adrenal gland in Callithrix jacchus

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
D. M. Renquist, Chief, PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
Developmental Endocrinology Branch, NICHD

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.3	.1	.2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Callithrix jacchus is being investigated as an animal model for the study of fetal adrenal regression, an involutional process in which there appears to be a disappearance of dehydroepiandosterone (DHA), the major steroid secreted by the fetal adrenal gland.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 00063-03 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Glucocorticoid Studies in Squirrel Monkeys (S. sciureus)

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
D. M. Renquist, Chief, PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
Developmental Endocrinology Branch, NICHD

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .6	PROFESSIONAL: .2	OTHER: .4

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The squirrel monkey is being studied to determine its usefulness as an animal model for hypercorticolism in humans through determination of its glucocorticoid serum levels and glucocorticoid receptors and the relations of these hormones to cortisol resistance.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00065-02 VR

PERIOD COVERED

October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Diet on Cataract Incidence in Rats with Heredity Retinal Dystrophy

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*

(Name, title, laboratory, and institute affiliation)

J.J. Knapka, Nutritionist, VRB, DRS

COOPERATING UNITS *(if any)*

Retinal and Ocular Corrective Tissue Diseases Section, Clinical Branch, NEI

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .35	PROFESSIONAL: .10	OTHER: .25

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A series of studies designed to identify dietary constituents affecting cataract incidence in rats with heredity retinal dystrophy are being conducted. Various types of diets differing in ingredient composition have been evaluated. The age of onset and the incidence of cataract can be influenced by dietary changes. For instance, virtually no cataracts were observed in rats up to 12 months of age when they were fed a purified diet with casein as the protein source. When fishmeal was used instead of casein as the protein source cataracts were observed in 100% of the rats by the time they were 56 days of age. It appears that there is a correlation between the dietary calcium concentration and the cataract incidence. New studies have been initiated using purified diets with graded levels of calcium and total minerals in order to verify this correlation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00066-02 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Effect of Diet on the Incidence of Stroke in Rats

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
J.J. Knapka, Nutritionist, SAS, VRB, DRS

COOPERATING UNITS *(if any)*
Biochemical Pharmacology Section, Hypertension-Endocrine Branch, Division of Interanimals Research, NHLBI

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.5	.1	.4

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A series of studies designed to identify factors influencing the incidence of stroke in the stroke-prone rat strain are in progress. A natural ingredient diet manufactured in accordance with a formulation obtained from Japan and reported to produce a high incidence of stroke in this rat strain, as well as purified diets varying in casein and salt are being evaluated. Preliminary analyses of the data indicate a high percentage of the stroke-prone rats die before they are 15 months old irrespective of diet. However, the primary cause of death was congestive heart failure rather than stroke. The diet made in accordance with the Japanese formulation had no effect on the death rate of the rats. Rats fed diets containing 10 or 30% casein died sooner than those fed a 20% concentration and rats fed 5 or 2.5% dietary salt died sooner than those fed 0.25%.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00067-01 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Hematologic and Serum Chemical Characteristics of Aotus sps.

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Dennis Barnard, Biologist, PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: .2	PROFESSIONAL: .2	OTHER: 0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Hematologic and serum chemical characteristics of 120 Aotus monkeys were determined to acquire information which may be useful in the care of these animals. In addition this information may have some bearing on the usefulness of the Aotus monkey as a lab animal model. The monkeys were bled every four months for one year. The hematologic and serum chemical characteristics are to be collected and statistically analyzed in the future.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00068-01 VR

PERIOD COVERED
March 21, 1983, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Zinc Deficiency in S. mystax and its relationship to Wasting Marmoset Syndrome

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)
Dennis Barnard, Biologist, PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
Small Animal Section, VRB, DRS

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.4	.30	.10

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study is to determine if the etiology of Wasting Marmoset Syndrome (WMS) is related to zinc deficiency. The clinical symptoms of zinc deficiency and WMS are very similar. It has been determined that the S. mystax are very zinc deficient. The study will involve feeding two diets to several wasting S. mystax, one diet will be supplemented with zinc and the other will not be. Serum zinc titers and blood chemistries will be sampled on a regular basis. Tissues will be taken from tamarins that die for zinc analysis.

The S. mystax is an invaluable lab animal model for infectious disease study. However, in captivity, these tamarins are unable to breed and eventually die due to WMS. The fact that S. mystax are zinc deficient may provide an answer to the etiology of WMS.

PHS 6040 (Rev. 1/83) GPO 895-100

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 RS 00069-01 VR

PERIOD COVERED
October 1, 1982, to September 30, 1983

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Anthropometric Study of the Aotus grisemembra and Aotus trivirgatus

PRINCIPAL INVESTIGATOR *(List other professional personnel on subsequent pages.)*
(Name, title, laboratory, and institute affiliation)

D. M. Renquist, Chief, PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.10	.10	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study is to establish anthropometric parameters for assessing normal growth of Aotus monkeys in captivity, to assess alterations in the development of experimentally treated animals, and to provide an age estimation for primates with unknown birth dates. The anthropometric and dental data collections were made on a regular basis until the animals reached maturity. The anthropometric measurements entailed, head length, head breadth, crown-rump length, foot length, hand length, bitrochanteric diameter and overall length. Thus far it has been determined that weights at six months were between 402 and 563 grams, approximately half that of the adults. Deciduous tooth eruption patterns are similar to other nonhuman primates. It has been observed that the growth rate plateaus at one year and six months of age. The anthropometric measurement correlating most closely with increasing age is the bitrochanteric diameter.

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